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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/872,250	06/01/2001	Gary S. Grubb	AM100058	4735

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EXAMINER	
HUI, SAN MING R	
ART UNIT	PAPER NUMBER
1617	

DATE MAILED: 02/12/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/872,250	Applicant(s) GRUBB, GARY S.	
	Examiner San-ming Hui	Art Unit 1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-11 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-11 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 3 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nordette® monograph (Physicians' Desk Reference, 50th edition, 1996, page 2755-2758) and Alesse® monograph (electronic Physicians' Desk Reference, April, 1997) in view of Katzung (Basic & Clinical Pharmacology, 6th edition, 1995, page 620) and Endrikat et al. (Contraception, 1997;55(3): 131-137), references of record in the previous Office Action mailed August 24, 2001.

Nordette® monograph teaches that an oral contraceptive composition containing 0.15mg of levonorgestrel and 30μg of ethinylestradiol (See page 2755, col. 3, Description Section). Nordette® monograph also teaches that breakthrough bleeding and spotting are sometimes experienced in patients who taking oral contraceptives in the first three months of use (See page 2757, col. 2, fourth paragraph).

Alesse® monograph teaches that an oral contraceptive composition containing 0.1mg of levonorgestrel and 20μg of ethinylestradiol (See first page, Description Section).

The references do not expressly teach the two compositions can be used in an oral contraceptive starter kit. The references do not expressly teach the kit contains

written instructions describing the order of use of the cycle packs. The references do not expressly teach the use of norethindrone, northindrone acetate, gestodene, and norgestimate in an oral contraceptive composition and kits.

Katzung teaches that norethindrone, northindrone acetate, and norgestimate are useful in oral contraceptive composition (See particularly page 620, Table 39-3, col. 3).

Endrikat et al. teaches that an oral contraceptive composition containing 20μg of ethinylestradiol and 75μg of Gestodene (See abstract). Endrikat et al. teaches that when the dose of ethinylEstradiol is lower, the rate of unwanted bleeding becomes higher (See the abstract).

It would have been obvious to one skill in the art when the invention was made to incorporate both Nordette® and Alesse® together with a written description of how to take the oral conceptive into a kit for oral contraception.

It would have been obvious to one skill in the art when the invention was made to employ different progestins such as norethindrone, northindrone acetate, gestodene, and norgestimate into an oral contraceptive composition and kit.

One of ordinary skill in the art would have motivated to incorporate both Nordette and Alesse together with a written description of how to take the oral conceptive into a pharmaceutical kit for oral contraception because combining two compositions which are known to be useful for oral contraception individually into a single pharmaceutical kit useful for the very same purpose is prima facie obvious, absent evidence to the contrary. See *In re Kerkhoven* 205 USPQ 1069. Furthermore, the inclusion of a written instruction including "indications and use" of the pharmaceutical composition is

mandated by 21 CFR 201.57 and is therefore obvious to one of ordinary skill in the art, absent evidence to the contrary.

One of ordinary skill in the art would have motivated to employ different progestins such as norethindrone, northindrone acetate, gestodene, and norgestimate into an oral contraceptive composition and kit because norethindrone, northindrone acetate, gestodene, and norgestimate are known to be useful in an oral contraceptive composition. The combining two agents which are known to be useful to oral contraception individually into a single composition useful for the very same purpose is prima facie obvious, absent evidence to the contrary. See *In re Kerkhoven* 205 USPQ 1069. In addition, the teaching of Nordette monograph and Endrikat provide a further motivation to combine the two known oral contraceptive products, Nordette and Alesse, with the estradiol level is higher in Nordette than that of Alesse in a single oral contraceptive starting kit. It is known in the art that the incidence of breakthrough bleeding is higher in the patients who receive a lower dose of ethinylestradiol. It is also known in the art that patients who take oral contraceptives in their first three months of use have a higher incidence of breakthrough bleeding. Therefore, giving patients, who start the oral contraceptive for the first time, an oral contraceptive product with a higher dose of ethinylestradiol in order to reduce the breakthrought bleeding initially in their first three months of using the oral contraceptives would be obvious based on the teaching of Nordette monograph and Endrikat. The subsequent lowering of estrogen dosage herein would have been obvious since it is well-known in the art that long term administration of estrogen would increase the risk of developing adverse effects such as

breast cancer (See Goodman and Gilman's the Pharmacological Basis of Therapeutics, 9th ed., page 1420-1421).

It is applicant's burden to demonstrate unexpected results over the closest prior art. See MPEP 716.02, also 716.02 (a) - (g). Furthermore, the unexpected results should be demonstrated with evidence that the differences in results are in fact unexpected and unobvious and of both statistical and practical significance. *Ex parte Gelles*, 22 USPQ2d 1318, 1319 (Bd. Pat. App. & Inter. 1992). Moreover, evidence as to any unexpected benefits must be "clear and convincing" *In re Lohr*, 137 USPQ 548 (CCPA 1963), and be of a scope reasonably commensurate with the scope of the subject matter claimed, *In re Linder*, 173 USPQ 356 (CCPA 1972). In regard to any possible unexpected result presented in the instant application, the specification, the examples at pages 5-12 has been considered but not found persuasive as to the presence of unexpected result. The examples merely demonstrate the different compositions containing different progestins components. No result as to the unwanted breakthrough bleeding is demonstrated.

Response to Remarks

Applicant's arguments filed November 21, 2001 regarding the pharmaceutical kit of the present invention resulting in lower incidence of unwanted breakthrough bleeding have been fully considered but they are not persuasive because, as discussed above, there is no comparative data or evidence on the record demonstrating that the claimed

invention has an unexpected effect over the cited prior art in lowering the incidence of unwanted breakthrough bleeding.

Applicant's remarks, filed November 21, 2001, that "for obviousness to lie over a reference, one skilled in the art must be motivated to make the invention in question based on something that is specifically taught in the reference" has been considered but is not found persuasive because, according to the MPEP 2143.01, obviousness can be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found **either** in the references themselves **or** in the knowledge generally available to one of ordinary skill in the art. *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988); *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). Therefore, the motivation to combine the teachings of the prior art is not necessarily found specifically in the references alone. The motivation for combining the teachings of the cited prior art can also be found in the knowledge generally available to one of ordinary skill in the art. In the instant case, both Nordette and Alesse are known to one of ordinary skill in the art to be useful for oral contraception. Combining both agents which are known to be useful in oral contraception individually into a single composition useful for the very same purpose is *prima facie* obvious, absent evidence to the contrary. In addition, the teaching of Nordette monograph and Endrikat provide a further motivation to combine the two known oral contraceptive products, Nordette and Alesse, with the estradiol level is higher in Nordette than that of Alesse in a single oral contraceptive starting kit. It is known in the art that the incidence of breakthrough bleeding is higher in the patients

who receive a lower dose of ethinylestradiol. It is also known in the art that patients who take oral contraceptives in their first three months of use have a higher incidence of breakthrough bleeding. Therefore, giving patients, who start the oral contraceptive for the first time, an oral contraceptive product with a higher dose of ethinylestradiol in order to reduce the breakthrought bleeding initially in their first three months of using the oral contraceptives would be obvious based on the teaching of Nordette monograph and Endrikat. The subsequent lowering of estrogen dosage herein would have been obvious since it is well-known in the art that long term administration of estrogen would increase the risk of developing adverse effects such as breast cancer (See Goodman and Gilman's the Pharmacological Basis of Therapeutics, 9th ed., page 1420-1421).

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). In the instant case, both Nordette and Alesse are known to one of ordinary skill in the art to be useful for oral contraception. Combining both agents as applicants have herein which are known to be useful to oral contraception individually into a single composition useful for the very same purpose is *prima facie* obvious, absent evidence to the contrary.

Applicant asserts that the Office is taking a position that it is obvious for one skilled in the art to take several cycles of Nordette followed by switching to Alesse to achieve the claimed invention. This is not however, the office position. The office position is that taking two or more pharmaceutical products which are individually known to be useful for oral contraceptive together and form a single product for the very same purpose is *prime facie* obvious regardless of how the claimed combination product, may be used or administered absent evidence to the contrary. Applicant's remarks regarding nonobviousness on this basis have been considered but are also not found persuasive because 1) the instant claims are drawn to a pharmaceutical kit, not a method of administering a composition or kit in order to reduce unwanted breakthrough bleeding; and 2) the instant claims do not recite the specific limitations on how to use the pharmaceutical kits to lower the incidence of unwanted breakthrough bleeding. It is further noted in this regard that the claims are drawn to kit products. Therefore, any claimed limitations reciting steps for administering these kits in order to achieve desired effects would be seen as not further limiting to the claimed kit.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the

shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to San-ming Hui whose telephone number is (703) 305-1002. The examiner can normally be reached on Mon 9:00 to 1:00, Tu - Fri from 9:00 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Minna Moezie, J.D., can be reached on (703) 308-4612. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4556 for regular communications and (703) 308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

San-ming Hui
February 8, 2002

MINNA MOEZIE, J.D.
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600